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Joseph M Skerpon
Banner & Witcoff Ltd
1001 G Street NW
Washington, DC 20001-4597

EXAMINER

JAGOE, DONNA A

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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Paper No. 04062004

Application Number: 09/402,634
Filing Date: March 27, 2000
Appellant(s): RONI KER ET AL.

Joseph M. Skerpon
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 08 January 2004.

(1) *Real Party in Interest*

A statement identifying the real party in interest is contained in the brief.

(2) *Related Appeals and Interferences*

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) *Status of Claims*

The statement of the status of the claims contained in the brief is incorrect. A correct statement of the status of the claims is as follows:

Claims 32 and 34-39 are withdrawn from consideration as not directed to the elected group.

Claims 13, 15-17, 19-24, 25-31, 40-43, 45-52, 54-62 and 64-68 stand finally rejected.

Claims 1-12, 14, 18, 25, 33, 44, 53 and 63 been canceled.¹

¹ The examiner inadvertently included those claims withdrawn from consideration in the Advisory Action dated 12/8/2003, however, in paper number 19, the restriction requirement was imposed and those claims withdrawn from consideration are clearly indicated in the office action of paper number 24, mailed 4/8/03.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is substantially correct. The changes are as follows: Appellant seems to be confused by the proceedings in this examination. For the sake of clarification to the appellant, the examiner will give a brief history of the prosecution.

1. 5 June 2001: 12 claims drawn to methods of preventing inflammation related cardiovascular disorders are presented. Examiner imposes a restriction requirement drawn to group I (claims 1-9) and group II (claims 10-12). Additionally, an election of species is imposed for A) species of cardiovascular disorders; B) compounds of claims

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5 and 8; C) substituents of compound I of claims 5,6 and 7; and D) R₄ substituents of compound II of claims 10 and 11.

2. 5 September 2001: Appellant responds by adding new claims 13-39, drawn to "the combination therapy invention" which includes new claims drawn to compositions and further new claims drawn to COX-2 inhibitors used in combination with an agent selected from the group consisting of (1) a lipid lowering drug; (2) an anti-oxidant; (3) a IIbIIIa antagonist; (4) an aldosterone inhibitor; (5) an AII antagonist (6) a β blocker; (7) aspirin; (8) a loop diuretic and (9) an ACE inhibitor. In response to the restriction/election requirement made, appellant argues that the inventions of group I and group II are partially overlapping and thus are not unrelated and elects group I with traverse. Appellant further elects (A) atherosclerosis; (B) 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide (of claims 5 and 8) and (C) the unsaturated heterocycle of claims 5, the 5- or 6 member unsaturated heterocycle of claim 6 and the pyrazolyl of claim 7 and (D) the haloalkyl of claim 10 and the lower haloalkyl of claim 11.

3. 8 November 2001: Examiner finds the appellants arguments regarding the restriction requirement persuasive and withdraws the restriction requirement. Claims 1-12 are rejected as unpatentable over WO 95/15316 and claims 1-39 are rejected as obvious over WO 95/15316 in view of the Merck Manual.

4. 15 January 2002: Appellant requests personal interview. Claims discussed are 1-39. Appellant asks examiner to restrict composition claims from method claims. Appellant indicates that he intends to cancel claims 1-12. Appellant brings 6,245,797 Winokur et al. to examiner's attention, citing potential interference over composition claims with statins combined with COX-2 inhibitors.

5. 4 February 2002: Appellant amends the application to correct 112 2nd paragraph rejections. Pending claims are now 13, 15-24, 26-32 and 34-39. Appellant again reminds the examiner regarding the Winokur et al. '797 patent, but fails to respond to the outstanding 35 U.S.C. §103(a) rejection. The outstanding 35 U.S.C. §102(b) rejection is moot due to cancellation of claims 1-12.

6. 23 April 2002: Examiner sends Appellant a letter stating a rejection was made in paper number 13 over Searle and Co. in view of the Merck Manual under 35 USC § 103(a) and Appellant should submit an argument pointing out disagreements with the examiner's contentions.

7. 17 May 2002: Appellant responds by asserting that a response was not necessary because claims 1-12 have been cancelled. Again Appellant reminds the examiner of the patent issued to Winokur (6,245,797) and wished to "underscore the patentability of the subject matter embraced by applicants pending amended claims since the subject matter had already been considered to be patentable by the USPTO."

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Appellant argues the obvious rejection citing improper hindsight evaluation of the invention.

8. 23 May 2002: Appellant sends an additional response adding new claims 40-68 drawn to prevention of pre-clinically evident cardiovascular disorders, preventing onset of a clinically evident cardiovascular disorder and treating a subject at risk of developing a cardiovascular disorder with an effective amount of a COX-2 inhibitor and a lipid lowering drug "in order to maintain a clear line of demarcation between this application and applicant's co-pending application (sic), SN 09/946,623 and avoid a "double patenting" rejection in that case".

9. 13 August 2002: Examiner imposes a restriction requirement drawn to group (I) methods of prophylaxing a subject from a cardiovascular disorder comprising administering a COX-2 inhibitor or a pharmaceutically acceptable salt thereof and a lipid lowering agent (claims 13, 15-24, 26-31 and 40-68) and group (II) compositions comprising a single formulation comprising a combination of a COX-2 inhibitor or a pharmaceutically acceptable salt thereof and a lipid lowering agent. Additionally, a 112^{1st} paragraph written description rejection is made over new claims 40-58 drawn to prevention of pre-clinically evident cardiovascular disorders and preventing onset of a clinically evident cardiovascular disorder.

10. 3 December 2002: Appellant claims to be confused. Appellant again reminds the examiner of the existence of the '797 patent and uses it as a basis for the patentability of the subject matter in the instant case. Appellant elects the method claims of Group I with traverse. Appellant seems to bristle at this restriction requirement, when at the interview on 15 January 2002, appellant asks the examiner to restrict methods from compositions. Appellant further elects atherosclerosis as the cardiovascular disorder, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide as the COX-2 inhibitor and a statin as the lipid lowering agent.

With regard to the 112 1st paragraph rejection for written description, appellant argues that the instant specification at page 3 is directed to preventing cardiovascular disorders in a subject in need of such prevention. At line 23 *et seq.* it defines the term "prevention" as to include either preventing the onset of clinically evident cardiovascular disorders altogether or preventing the onset of a preclinically evident stage of cardiovascular disorder in individuals. This includes prophylactic treatment of those at risk of developing a cardiovascular disorder. Appellant argues regarding the outstanding 102(b) rejection and the outstanding 103(a) rejection and even again points out the patent issued to Winokor et al. (6,245,797) as evidence of the "patentability of the subject matter embraced by applicants' pending claims".

11. 8 April 2003: Examiner acknowledges appellants' election of group I with traverse and claims 32 and 34-39 are withdrawn from further consideration. The rejection of claims 40-58 under 112 1st paragraph written description is maintained and

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claims 40, 49 and 59 are additionally rejected under 112 1st paragraph for enablement of the claims. Appellant is instructed that arguments regarding the '797 patent issued to Winokur et al. will not be addressed since each patent application is examined on its own merits. Arguments are addressed regarding the prior art rejection, especially with regard to the accusation of hindsight reasoning. Rejection is made final.

12. 18 July 2003: Appellant requests personal interview wherein alternatives to "preventing" language is discussed and Appellant claims to be confused by the prior art rejections. U.S. Patent No. 5,776,984 issued to Dellaria is discussed as it was applied in the related case. Appellant requests yet another non-final office action be issued.

13. 8 August 2003: Appellant replies to final office action with amendments to claims 13, 40, 49 and 59 and cancellation of claims 18, 44, 53 and 63 and confirms withdrawal of composition claims 32 and 34-39. Appellant asserts that rejection of claims 1-12 under 35 USC 102(b), rejection of claims 17-23, 28-31 and 36-39 under 112 2nd paragraph, and claims 40-58 under 35 USC §112 1st paragraph have all been withdrawn. Appellant argues regarding the rejection of claims 40, 49 and 59 under 35 USC §112 1st paragraph as not being enabled. Appellant again cites US 6,245,797 as "evidence of the utility/enablement of the subject matter embraced by the pending claims". Appellant again accuses the examiner of "improper hindsight evaluation" regarding the outstanding 35 USC 103(a) rejection.

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14. 8 December 2003: Advisory action issued wherein amendments to the claims are entered, but does not place the application in condition for allowance because: In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

15. Appellant writes brief on appeal.

(7) *Grouping of Claims*

Appellant's brief includes a statement that claims:

- I) 13, 15-17, 32, 34, 40-43, 49-52, 55, 59-62 and 65
- II) 19 and 20-24, 26-31, 45-48, 54, 56-58, 64 and 66-68
- III) 35-39

do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

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The appellant's statement in the brief that certain claims do not stand or fall together is not agreed with because composition claims 32 and 34-39 have been withdrawn from further consideration.

(8) *Claims Appealed*

A substantially correct copy of appealed claims appears on pages i-xiv of the Appendix to the appellant's brief. The minor errors are as follows:

Claims 32 and 34-39 have been withdrawn from further consideration.

(9) *Prior Art of Record*

WO 95/15316 G.D. Searle & Co., 8 June 1999

<http://www.merck.com/mrkshared/mmanual/section2/chapter15/15a.jsp>

(10) *Grounds of Rejection*

The following ground(s) of rejection are applicable to the appealed claims:

1. Claims 13, 15-17, 19-24, 25-31, 40-43, 45-52, 54-62 and 64-68 stand finally rejected under 35 U.S.C. 103(a). This rejection is set forth in prior Office Action, Paper No. 13. and repeated below.

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Claims 1-39 (claims now pending are 13, 15-17, 19-24, 25-31, 40-43, 45-52, 54-62 and 64-68) are rejected under 35 U.S.C. 103(a) as being unpatentable over Searle and Co. WO 95/15316 A in view of the Merck Manual. The claims are drawn to prophylactic treatment of a subject at risk of developing a cardiovascular disorder comprising treating a subject with a COX-2 inhibitor and, *inter alia*, a lipid lowering drug such as a statin.

Searle and Co. teach that COX-2 inhibitors would be useful for conditions such as vascular disease and myocardias ischemia and the like (page 7, lines 8-36). The Merck Manual teaches that HMG-COA reductase inhibitors (statins) can lower LDL levels and prevent unstable angina and MI and decrease the need for surgical coronary revascularization. It differs from the instant application in that it does not explicitly teach that these two agents be given together. It is *prima facie* obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. *In re Kerkhoven* 205 USPQ 1069. Motivation for combining said compositions flows logically from their having been individually taught in the prior art. *In re Crockett* 126 USPQ 186, 188. See also *In re Shannon* 148 USPQ 504 (one step laminate is obvious from two step laminate).

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(11) Response to Argument

Appellant accuses the examiner of improper hindsight construction of the separate teachings of WO 95/15316 (hereafter "Searle WO publication") and the Merck Manual, section 2, Chapter 15, Hyperlipidemia (hereafter "Merck"). In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Appellant asserts that the Searle WO publication teaches that the recited compounds, a particular class of selective COX-2 inhibitors are useful for treatment of inflammation in such diseases as vascular diseases...myocardial ischemia and the like. Appellant asserts that the examiner has made an over-generalization. In response, the examiner turns to the instant specification to shed light on the nature if the instant invention. Page 2, lines 3-9 of the instant specification discloses that the role of inflammation in cardiovascular disease is becoming more understood. Ridker et al. teach a possible role of inflammation in cardiovascular disease and J. Boyle teaches the association of plaque rupture and atherosclerotic inflammation. Further, page 2, last full paragraph recites the COX-2 inhibitors of the instant invention useful for the prevention of **inflammation related**

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cardiovascular disorders. If there is pathway other than treatment of inflammation, used to treat the instantly claimed cardiovascular disorders, it is not described in appellants' specification.

Appellant charges that the case law cited in the 103(a) rejection is not germane to the current circumstance. In *Crockett*, one of the cited references taught using magnesium oxide and the other taught using calcium carbide for the very same purpose, i.e., to promote the formation of a nodular structure in cast iron, *Crockett* at 188. In the instant case, drawn to COX-2 inhibitors combined with lipid lowering agents to treat/prevent cardiovascular disease i.e. atherosclerosis. The cited "Searle WO publication" teaches using COX-2 inhibitors and the cited "Merck" reference teaches using lipid lowering agents for the very same purpose, i.e., to treat/prevent vascular disease e.g. atherosclerosis.

In response to appellants argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, since it is known that anti-inflammatories such as COX-2 inhibitors treat inflammation related **vascular disease** and **myocardial infarction** and since it is known from the teaching of "Merck" that lipid lowering agents reduce the formation of plaque on blood vessels which would

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lead to the inflammation related vascular disease of the Searle WO Publication, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine these two agents to treat a vascular disease such as atherosclerosis (a vascular disease).

Regarding the issuance of U.S. 6,245,797, this argument will not be addressed since each patent application is examined on its own merits and the examiner is presently prosecuting the instant application based on its own merits, not the merits of the '797 patent.

In response to applicant's argument that there is nothing in the primary reference (Searle WO publication) that remotely indicates that COX-2 inhibitors would be useful for lowering cholesterol, it is noted that the features upon which applicant relies (i.e., lowering cholesterol) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to applicant's argument that there is nothing in the "Merck" reference suggesting statins would be useful for treating inflammation, it is noted that the features upon which applicant relies (i.e., lowering cholesterol) are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In further response, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the

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structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,


Donna Jagoe
Patent Examiner
Art Unit 1614



MARIANNE C. SEIDEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

dj
April 8, 2004

Conferees



SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER

THOMAS F PETERSON
LADAS & PARRY
224 SOUTH MICHIGAN AVENUE
CHICAGO, IL 60604